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A CONVENIENT CONVERSION OF ALDOXIMES TO NITRILES UNDER PHASE-TRANSFER CONDITIONS

Hiraku SHINOZAKI,* Mari IMAIZUMI, and Moritaka TAJIMA
Department of Applied Science, Tokyo Denki University,
Kanda, Tokyo 101

A variety of aldoximes were converted into the corresponding nitriles by using carbon disulfide as dehydration reagent under phase-transfer conditions. One-pot syntheses of nitriles from aldehydes are also described.

The dehydration of aldoximes to nitriles is commonly accomplished by using reagents such as phosphorus pentoxide, triethyl phosphate, and acyl chloride.[1] This conversion, however, usually requires anhydrous conditions.

Recent syntheses of nitriles from aldoximes have used the new reagents which effect the efficient dehydration under mild conditions. For example, amides and aldoximes were dehydrated by dichlorocarbene generated from chloroform under phase-transfer conditions[2] or by trifluoroacetic anhydride.[3] Aldoximes were also dehydrated by dicyclohexylcarbodi-imide[4] or N-trifluoroacetylimidazole.[5] Aldehydes can also be converted into nitriles by refluxing in formic acid in the presence of hydroxylamine hydrochloride.[6]

In the present paper we wish to report a new method which uses carbon disulfide as dehydration reagent under phase-transfer conditions and converts aldoximes into nitriles.

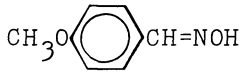
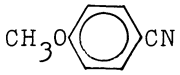
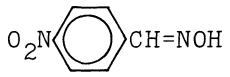
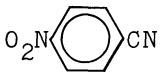
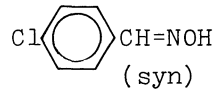
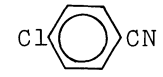
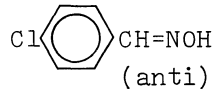
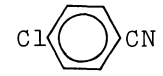
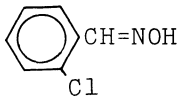
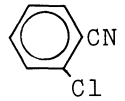
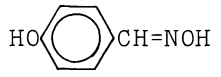
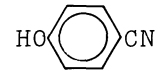
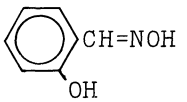
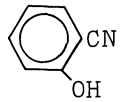
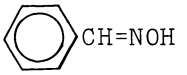
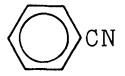
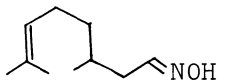
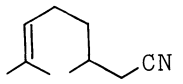
$$\text{R-CH=NOH} \xrightarrow[n\text{-Bu}_4\text{N}^+\text{HSO}_4^-,\ \text{aq NaOH}]{\text{CS}_2,\ \text{C}_6\text{H}_6} \text{R-CN}$$

The reaction was carried out by stirring a mixture of an aldoxime, carbon disulfide, tetrabutylammonium hydrogensulfate, benzene, and 15% aqueous sodium hydroxide. The reaction conditions and yields are summarized in the Table 1 which shows the usefulness and the versatility of this new synthetic method.

Table shows that both syn and anti-p-chlorobenzaldoximes give comparable yields of the nitriles. Dehydration of aromatic aldoximes containing a hydroxyl group or aliphatic aldoximes having a carbon-carbon double bond, which can not attained by dichlorocarbene method,[2] is satisfactorily done by this method.

The effect of phase-transfer catalyst was examined with cinnamaldoxime. After 3 h, the nitrile was obtained in 86% yield in the presence of the catalyst, while in the absence of the catalyst only 30% yield of the nitrile was produced.

Table 1. Preparation of Nitriles from Aldoximes[a)]

Substrate	Reaction time/h	Product	Yield/%
	0.5		90[b)]
	0.5		78[b)]
 (syn)	0.5		72[b)]
 (anti)	0.5		85[b)]
	0.5		70[b)]
	1.5		80[b)]
	1.5		77[b)]
	19		80[c)]
$CH_3(CH_2)_5CH=NOH$	5	$CH_3(CH_2)_5CN$	64[c)]
	20		83[c)]

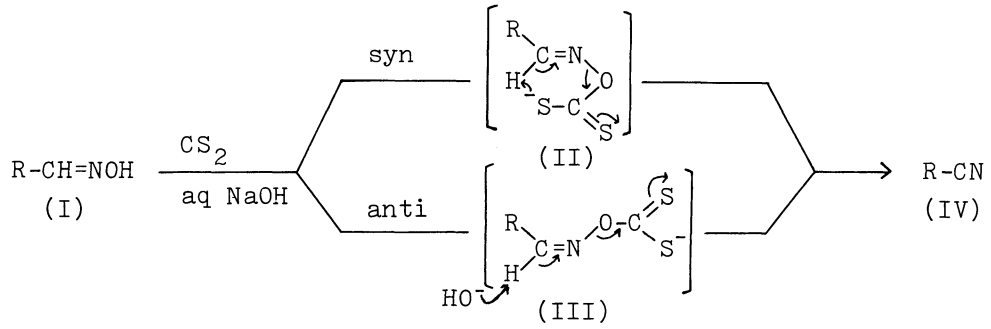
a) All aldoximes and nitriles had their physical and spectral properties identical to those of the authentic compounds. b) The reaction was done in a 1 mmol scale, and yield based on products isolated by column chromatography. c) The reaction was done in 20 mmol scale, and yield based on distilled products.

A typical procedure:

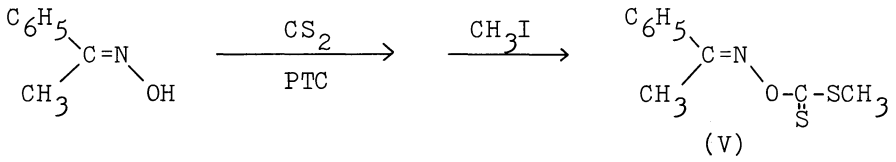
To a solution of 4-methoxybenzaldoxime (0.151 g, 1.0 mmol), $Bu_4N \cdot HSO_4$ (0.05 g, 0.15 mmol), and CS_2 (0.4 ml, 6.6 mmol) in 2 ml of benzene was added dropwise 1 ml of 15% aq NaOH. The mixture was stirred for 0.5 h at room temperature. The organic layer was separated and the aqueous layer was extracted with benzene. The combined organic layer was dried over sodium sulfate and concentrated under reduced pressure. Chromatography of the residue of Florisil (CH_2Cl_2-hexane) gave 4-methoxybenzonitrile (0.120 g, 90%).

In the case of 2- and 4-cyanophenols, the aqueous layer was extracted with dichloromethane after acidification with concentrated hydrochloric acid.

By analogy to the mechanism proposed for the Chugaev reaction, the dehydration reaction may proceed as follows:



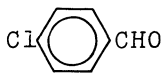
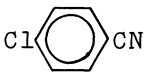
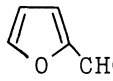
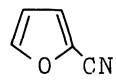
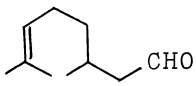
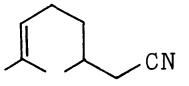
Oxime anion would react with carbon disulfide in organic layer to yield intermediates (II) or (III), which would produce nitrile (IV) by elimination of COS_2^{2-}. In fact, the intermediate was captured by methylation with methyl iodide in the case of acetophenone oxime; the reaction afforded the dithiocarbonate (V) in 85% yield.[7] This fact supports the formation of intermediate (II) or (III).



We also examined a one-pot procedure for the syntheses of nitriles from aldehydes. Aldehyde, hydroxylamine hydrochloride, phase-transfer catalyst, carbon disulfide, aqueous sodium hydroxide, and benzene were mixed, and we obtained nitriles in low yields. However, the yields were improved by adding carbon disulfide after the completion of oximation. The reaction conditions and yields are summarized in the Table 2.

The procedure developed here is simple and provides a new convenient method for the syntheses of nitriles.

Table 2. Preparation of Nitriles from Aldehydes

Substrate	Reaction[a] time/h	Product	Yield/%	bp/°C
	0.5 2.0		72[b]	
C_6H_5-CHO	0.5 2.0	C_6H_5CN	53[c]	76-79 20 mmHg
$CH_3(CH_2)_4CHO$	0.5 18	$CH_3(CH_2)_4CN$	36[c]	55-56 18 mmHg
	0.5 2.0		35[c]	140-150 bulb to bulb
	2.5 5.0		75[c]	103-105 15 mmHg

a) The first column is a time needed for oximation and the second is one needed for nitrile formation. b) The reaction was done in a 1 mmol scale, and yield based on products isolated by column chromatography. c) The reaction was done in 20 mmol scale, and yield based on distilled products.

A typical one-pot procedure:

A mixture of citronellal (3.05 g, 20 mmol), hydroxylamine hydrochloride (1.6 g, 23 mmol), $Bu_4N \cdot HSO_4$ (0.5 g, 1.5 mmol), 20 ml of benzene, and 30 ml of 15% aq NaOH was stirred for 0.5 h at room temperature. After oximation, 4 ml of carbon disulfide was added dropwise to the mixture cooled by a water bath. The reaction mixture was allowed to warm to room temperature and stirred for another 5 h. The organic layer was separated, and the aqueous layer was extracted with benzene. The combined organic layer was dried, evaporated, and purified by distillation to afford 2.25 g (75%, bp 103-105 °C/15 mmHg) of the corresponding nitrile.

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References

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7) mp 52-54 °C; PMR($CDCl_3$,δ) 7.60-7.24 (m, 5H, aromatic), 2.65 (s, 3H, CH_3S), and 2.25 (s, 3H, CH_3-C=N); Mass m/e, 225 (M^+); IR(KBr) 1620 (C=N) and 1150 (-OCS_2-).

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